UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/643,141	08/18/2003	Stephen L. Hutcherson	C01037.70049.US	3287

7590 02/27/2006

Helen C. Lockhart
Wolf, Greenfield & Sacks, P.C.
Federal Reserve Plaza
600 Atlantic Avenue
Boston, MA 02210

EXAMINER	
HUMPHREY, DAVID HAROLD	
ART UNIT	PAPER NUMBER
1643	

DATE MAILED: 02/27/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/643,141	HUTCHERSON ET AL.	
	Examiner	Art Unit	
	David Humphrey	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 26-48 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 26-48 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 08/18/03;02/06/04.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-25 are cancelled by the Applicants' amendment filed on August 18, 2003.

Claims 26-48 are added.

Claims 26-48 are examined on the merits.

Claim Rejections - 35 USC § 112, first paragraph

2. The following is a quotation of the first paragraph of 35 U.S.C. §112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 26-48 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **THIS IS A NEW MATTER REJECTION.** The claims have been amended to recite "not antisense" as a limitation, however, the addition of the term "not antisense" or "sense" for that matter, do not find support in the specification as filed. The specification refers to the use of sense phosphorothioate oligonucleotides in the background of the invention section when reporting the work of McIntyre et al. There is no specific contemplation in the detailed description or examples in the specification other than the description of the work of McIntyre et al. of the use of "not antisense" phosphorothioate oligonucleotide analogs and therefore the

specification does not provide support for the limitation "not antisense". The specification states "the present invention employs phosphorothioate antisense oligonucleotide analogs which elicit a local inflammatory response," see page 10, lines 16-18. Applicants are invited to specifically point out and disclose support for this term.

4. Claims 26-48 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was fled, had possession of the claimed invention.

The Written Description Guidelines for examination of patent applications indicates, "the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical characteristics and/or other chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show applicant was in possession of the claimed genus. " (See MPEP 2164).

The specification does not reasonably provide a written description for a method for stimulating an immune response in a human comprising administering an amount of a phosphorothioate oligonucleotide analog effective to stimulate an immune response. Thus, the full scope of the claims is a method that utilizes any phosphorothioate

oligonucleotide analog to stimulate an immune response. This encompasses a huge number of possible phosphorothioate oligonucleotide analog sequences.

It is art known that not all phosphorothioate oligonucleotides analogs elicit an immune response. In experiments using antisense oligonucleotides, sense oligonucleotides have frequently been used as a control for nonspecific effects, with variable results, see for example McIntyre et al. (Antisense Research and Development 3: 309-322, 1993; cited in Applicants' IDS). Some phosphorothioate oligonucleotides do not elicit nonspecific effects or immune responses. However, other phosphothioate oligonucleotides elicit a sequence-specific response. McIntyre KW et al. teach that phosphothioate oligonucleotides can exert sequence-specific effects in vivo, irrespective of sense and antisense orientation, see page 309, Abstract, last sentence. Nonspecific binding of phosphorothioate oligonucleotides may elicit a localized immune response but can also lead to cytotoxicity of normal cells. Wu CL et al. (Anesthesiology 94: 1119-1132, 2001), teach that phosphorothioates molecules may interact non-specifically with cellular targets, resulting in extensive cellular cytotoxicity, see page 1129, right column, first paragraph, last sentence. Therefore, upon administration of any phosphorothioate oligonucleotide analog, one could expect a wide variety of responses ranging from no response, a nonspecific cytotoxic response to both diseased and healthy cells, an increase in immune system sensitivity to other foreign antigens, a local immune response that may or may not be beneficial to the host, or a sequence-specific response that may or may not be beneficial to the host. As evidenced by the

references, the response due to the administration of a phosphorothioate oligonucleotide analog is sequence dependent.

To provide adequate written description and evidence of possession of a claimed genus, a phosphorothioate oligonucleotide that when administered to a patient elicits an immune response, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, and structure/function correlation. In this case, the only factor present is the sequence of three phosphorothioate oligonucletides analogs. Only one of these SEQ ID NO: 1, also referred to in the specification as ISIS 2105, an antisense phosphorothioate oligonucleotide analog, is administered to patients to elicit a local immune response, see Specification, Examples 9-12. Other than the three sequences SEQ ID NOs: 1, 2, and 3 (see Specification page 12, lines 7-9), only one of which was actually administered and shown to elicit a local immune response, no other sequences are provided that would indicate that Applicants are in possession of the genus of phosphorothioate oligonucleotide analogs that elicit an immune response. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus and one of ordinary skill in the art would conclude that Applicant was not in possession of the broadly claimed genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought,

he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116). As discussed above, the skilled artisan cannot envision the nucleotide sequences of the encompassed genus of phosphorothioate oligonucleotide analogs, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See Fiers v. Revel, 25 USPQ2d 1601 at 1606 (CAFC 1993) and Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016.

One cannot describe what one has not conceived. See Fiddes v. Baird, 30 USPQ2d 1481 at 1483. In Fiddes v. Baird, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

See University of Calfornia v. Eli Lilly and Co. 43 USPQZd 1398. Applicant is directed to the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, paragraph 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

5. Claims 26-48 are rejected under 35 U.S.C. §112, first paragraph, because the specification, while being enabling for a method of stimulating a local immune response in a human by administering one phosphorothioate oligonucleotide analog, ISIS 2105, does not reasonably provide enablement for a method of stimulating a humoral immune response in a human using any phosphorothioate oligonucleotide analogs in a patient with any type of cancer, any type of infection, and in combination with any type of surgery. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir,1988). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue' not 'experimentation'. " (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the breadth of the claims, (2) the nature of the invention, (3) the state of the prior art, (4) the level of one of ordinary skill, (5) the level of predictability in the art, (6) the amount of direction provided

by the inventor, (7) the existence of working examples, (8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The nature of the invention and the breadth of the claims: The instant claims are drawn to a method for stimulating an immune response in a human comprising administering to a human as an immunopotentiator, an amount of a phosphorothioate oligonucleotide analog, wherein the phosphorothioate analog is not antisense and is an immunopoteniator of an antibody response. Claims 28-30 recite the limitations wherein the human has cancer, an infection, or is having surgery. Claim 31 is drawn to the same method wherein the oligonucleotide analog is formulated in a vehicle selected from the group consisting of liposomes and cationic lipids. Claims 32-35 further limit the method to using an oligonucleotide wherein all of the linkages of the phosphorothioate analog are phosphorothioate linkages and the analog includes at least one 2'-O-alky modification (either 2'-O-methyl or 2'-O-propyl). Claims 36 and 37 further comprise administering a therapeutic modality such as a drug before, after, or simultaneously with the phosphorothioate oligonucleotide analog. Claims 38-48 recite essentially the same method but using the phosphorothioate oligonucleotide analog to stimulate a humoral immune response.

Therefore, the claims encompass a method to stimulate an immune response to enhance the efficacy of anti-cancer or anti-infective agents and that the humoral immune response which is stimulated by the claimed invention may be a T-cell mediated response and/or a B-cell mediated antibody response. Claims 26-37

encompasses methods for stimulating any type of immune response and claims 38-48 encompass methods for stimulating a humoral immune response wherein any dose of an oligo analog having as few as one phosphorothioate group is administered to any cell or tissue of a human. The term "oligonucleotide analog" according to the specification encompasses altered sugar moieties, inter-sugar linkages, altered base units or other modifications with the spirit of the invention. In addition, the analog may have additional modifications to enhance the uptake, stability, affinity or other features of the oligonucleotide and all such analogs are comprehended by this invention so long as function effectively to produce an immune response, see Specification, page 11, lines 12-35. Thus, the claims are very broad and encompass methods of using unspecified and untested phosphorothioate oligonucleotide analogs.

The state of the prior art and the predictability of the art: Allison et al. (Molecular Immunology 28: 279-284, 1991; cited in Applicants' IDS) teach that the efficacy of a stimulator of an immune response such as an adjuvant is judged by determining the types and levels of antibodies produced when an antigen is administered with the adjuvant, see page 279, right column, first complete paragraph, lines 1 and 2; that adjuvants differ in their capacity to elicit effective levels of antibodies with sufficiently high affinity to any given antigen; and they note that different types of antibodies which might be elicited in an adjuvant-dependent manner differ widely in their ability to confer protection to the host organism; for example, some adjuvant-specific IgG isotypes bind to monocyte receptors, interact with effector cells to elicit a cytotoxic response, confer protection against tumors, and protect against infectious agents, whereas other do not,

see page 280, left column, lines 2-6; and IgM antibodies do not pass between the vascular and extravascular compartments as easily as do IgG antibodies, see page 279, right column, bottom paragraph, lines 2-4.

The specification teaches that fully phosphorothioated oligos promote release of IL-1α from cultured keratinocytes whereas phosphodiester oligos do not, see page 16, lines 17-21; that daily intradermal injections into mice of 6.6 mg/kg/day of fully phosphorothioated oligo for 14 days causes an increase in spleen weight without stimulation of T-cell-dependent responses, see pages 24-25, Example 8; and that repeated intravenous injections of phosphorothoated oligos into mice and rats causes splenomegaly, see page 19, lines 30-32. The latter results do not appear to correlate with Iversen's teaching that daily intravenous injection into mice of a dose of 50 mg/kg/day of fully phosphorothioated oligos for 12 days did not cause any change in spleen weights, see Iversen, page 535, Repeated Daily Injections, second paragraph. The specification provides no evidence that administration of phophorothioate oligonucleotide analog can stimulate anything other than a local immune response. In addition, it is unclear whether this immune response actually enhances any therapeutic treatment or confers any therapeutic benefit. The only example of the effects of the claimed invention on antibody production, either in vivo or in vitro, given in the specification teaches that daily intradermal injections into rats of at least 3.3 mg/kg/day of fully phosphorothioated oligo for 14 days elicits increased production of IgM antibodies against T-cell-dependent sheep erythrocyte antigen on sheep RBCs, see pages 20, and 23-24. This increase in immune response to a T-cell independent

antigen in rats given an intradermal injection of the oligonucleotide analogs does not appear to correlate with the aforementioned failure of Applicant to observe stimulation of T-cell-dependent responses following repeated intradermal injection of the oligonucleotide into mice.

Mojcik et al. (Clinical Immunology and Immunopathy 67(2): 130-136, 1998; cited in Applicants' IDS), Branda et al. (Biochemical Pharmacology 45(10): 2037-2043, 1993; cited in Applicants' IDS), and McIntyre et al. (Antisense Research and Development 3:309-322, 1993; cited in Applicants' IDS) all teach that induction of splenomegaly and stimulation of B-lymphocyte proliferation in mice injected with phosphorothioate oligos occurs unpredictably in a manner that is dependent on the nucleotide sequence of the phosphorothioate oligonucleotide analogs, as these effects occur following injection of some phosphorothoate oligonucleotide analogs, but not upon injection of others; see Mojcik et al., page 130, Abstract, and page 134, left column, lines 1-4; see Branda et al., page 2037, Abstract, and page 2042, Discussion, lines 4-7; see McIntyre et al., page 309, Abstract. Further, Liang et al. (J. Clin. Invest. 98(5): 1119-1129, 1996) teach that although bacterial DNA and certain oligodeoxynucleotides can stimulate murine B cells, much less information is available on the immunostimulatory capacity of these materials for human B cells. Because of the differences in the responsiveness of human and murine B cells to certain stimuli, it is not possible to extrapolate results obtained from mouse to man, see page 1119, right column, third complete paragraph, lines 1-6.

The presence of an immune response seems to be largely dependent on the specific sequence of phosphorothioate oligonucleotide analog. Vollmer J. et al (Antisense and Nucleic Acid Drug Development, 12:165-175, 2002) teach specific sequence requirements of CpG-free phosporothioate oligodeoxynucleotides (ODNs) for *in vitro* immunostimulatory activity, specifically the thymidine content and the length of a phosporothioate-ODNs determine the immunostimulatory potential (see entire document). Vollmer et al teach that a polycytosine ODN (i.e., Py-rich), such as ODN 2178 (see Table 1) is essentially immunologiocally inert (see page 168, right column) and a short polythymidine ODN with 18 nucleotides showed background activity, whereas increasing the length resulted in a progressively strong increase in stimulation for polythymidine ODNs 2195 (21 bases), 2183 (24 bases), and 2194 (27 bases) (see page 169, left column and Figure 2). According to Vollmer et al, short non-CpG phosphorothioate ODN induces only minimal stimulation *in vivo* as well as *in vitro* and that ODNs equal or greater than 24 nucleotides are needed to induce stronger stimulation (see page 173, right column) and Vollmer et al states "Nevertheless, *in vitro* longer non-CpG T-rich ODNs are always less efficient and potent than CpG ODNs, and, therefore, they might induce weaker *in vivo* effects that are not sufficient to mediate efficiently a Th1-dominated immune response." The skilled artisan would not predict or anticipate that such a weak immunostimulatory response illicited by non-CpG T-rich ODNs as an effective treatment or preventative therapy for asthma, allergy, infectious disease and cancer. Vollmer et al teaches that the mechanism of immune activation by non-CpG ODNs remains to be elucidated. In agreement with the teachings of Vollmer,

McCluskie et al (Vaccine, 19:2657-2660, 2001) teaches a polythymidine nucleic acid twenty nucleotides in length (ODN 1983), which did not have an immunostimulatory effect in immunized mice (see page 2658 and Figures 1-2). Further, Jones et al (Vaccine, 17:3065-3071, 1999) teach a T-rich immunostimulatory nucleic acid lacking CpG dinucleotides as a negative control for testing ODNs *in vivo* for their adjuvant activities in monkeys (see page 3066, right column and page 3067 and Figures 1-2).

In view of the above, one skilled in the art at the time the invention was made would have considered the immune response of a human upon the administration of phosphorothioate oligonucleotide analgos to be uncertain and unpredictable, and that successful stimulation of an immune response in a treated patient would depend critically on the nature of the immune response in question, the cell or tissue of interest, the structure of the phosphorothioate oligonucleotide analog, and the dosage.

The amount of direction provided by the inventor and the existence of working examples: The amount of direction provided by the specification is very limited. No structural requirement or core structural elements are provided such as 5'-XXCGXX-3' for example, for the phosphorothioate oligonucleotide analogs are provided. The specification merely recites that the optimal length of the analogs is from about 15 to about 50 base subunits. The specification also does not contemplate the use of sense phosphorothioate sense oligonucleotide analogs other than to provide a summary others work in the background of the invention.

Demonstration of immune system stimulation or antibody production upon administration of a phosphorothioate oligonucleotide analog to humans is also lacking.

The specification provides no guidance regarding the extent to which the observed production of IgM antibody in rats elicited in the Example 7 would be expected to confer any therapeutic benefit to a human with an infection by a pathogen or with cancer or undergoing surgery. In view of the recognized state of unpredictability in the art of using a composition comprising a phosphorothioate oligonucleotide as an immunopotentiator as discussed above, one skilled in the art at the time the invention was made would not have considered the disclosed examples to be correlative with the successful use of the claimed invention to stimulate an immune response to enhance the efficacy of anti-cancer and anti-infective agents in target cells in vivo so as to provide a therapeutic benefit to a human patient. Therefore, the specification does not provide adequate guidance or correlatable working examples.

A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed inventions without undue experimentation. In re Wright, 27 USPQ2d 1510 (CAFC). The disclosure does not demonstrate sufficient evidence to support Applicants' claim to methods of administering any phosphorothioate oligonucleotide analog to elicit an immune response. All of the factors considered in the sections above, underscores the criticality of providing working examples in the specification for an unpredictable art.

Quantity of experimentation needed to make or use the invention based on the content of the disclosure: In view of the Wands factors considered above, one of ordinary skill in the art would conclude that methods of eliciting an immune response by

the administration of any phosphorothioate oligonucleotide analog would require undue experimentation in order to use the invention as claimed by the Applicants.

Double patenting

6. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

7. Claims 26, 28, 29, and 30, are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-8 of U.S. Patent No. 6,727,230 (Hutcherson et al.) in view of U.S. Patent 5,356,882 (Walker et al., effective filing date July 13, 1990).

Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant application contains the same steps required by the patent to generate an immune response. Furthermore, the patent recites a method to stimulate a cell-mediated immune response, which anticipates the more broadly claimed instant application to a method of stimulating an immune response. Since an immune response consists of a cell-mediated response and a humoral response, the claims of the patent anticipate the instant application.

Claims 26, 28, 29, and 30, of the instant application are drawn to a method for stimulating an immune response in a human comprising administering to a human an amount of a phosphorothioate oligonucleotide analog that is not antisense wherein the patient has cancer, an infection, or is having surgery. The claims also recite administration by a route selected from the group consisting of inhalation, ophthalmic, intranasal, parenteral, oral and intradermal.

Claims 1-8, of Patent '230 are drawn to a method for treating a human to stimulate a cell-mediated immune response comprising administering to an amount of a phosphorothioate oligonucleotide analog that is not antisense wherein the patient has cancer, an infection, or having surgery. Patent '230 does not teach routes of administration. This deficiency is made up for by the teachings of Patent '882.

Patent '882 teaches methods of administration of therapeutic nucleosides by various routes such as oral, nasal, parenteral including intradermal, see column 4, lines 49-57. Patent '882 also teaches administration routes such as eye drops or topical creams, see column 5, lines 64-67 and column 6, lines 55-58. Patent '882 teaches nasal administration by inhalation, see column 7, lines 5-16.

Therefore, it would have been *prima facie* obvious to combine the method of eliciting an immune response using phosphorothioate oligonucleotide analogs of Patent '230 with the administration methods of Patent '882 in order to deliver therapeutic compounds to the patient.

One of ordinary skill in the art would have been motivated with a reasonable expectation of success to combine the methods of Patent '230 and '882 since Patent '882 teaches effective doses and percent of active ingredient in the administered compositions depending on route for various routes of administration, see column 5, lines 37-45, lines 64-67, and column 6, lines 59-61 as representative examples.

Therefore, the specific method of the patent to elicit a cell-mediated immune response makes obvious the more general method of the instant application to elicit an immune response.

Conclusion

6. No claim is allowed.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Humphrey whose telephone number is (571) 272-5544. The examiner can normally be reached on Mon-Fri 8:30AM-5PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

LARRY R. HELMS, PH.D.
SUPERVISORY PATENT EXAMINER

David Humphrey, Ph.D.

February 15, 2006